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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 111903

Application Number: 09/800,103
Filing Date: March 06, 2001
Appellant(s): DONOHO ET AL.

Lance Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/23/03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. However, the Examiner brings to the Board's attention the following related cases on appeal which have similar issues: 09/775,685 and 09/770,643.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-3, 13 and 14 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Skolnick, J. et al. "From genes to protein structure and function: novel applications of computational approaches in the genomic era" Trends in Biotechnology, vol 18, no. 1 (2000), pp. 34-39.

Bork, P. "Powers and pitfalls in sequence analysis: the 70% hurdle" Genome Research, vol 10 (2000), pp. 398-400.

Doerks T. et al. "Protein annotation: detective work for function prediction" Trends in Genetics, vol 14, no. 6 (1998), pp.248-250.

Smith, TF. et al. "The challenges of genome sequence annotation or "the devil is in the details" Nature Biotechnology, vol 15 (Nov 1997), pp. 1222-1223.

Brenner, S. "Errors in genome annotation" Trends in Genetics, vol 15, no. 4 (April 1999), p. 132.

Bork, P. et al. "Go hunting in sequence databases but watch out for traps" Trends in Genetics, vol 12, no. 10 (Oct 1996), pp. 425-427.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

Claims 1-3 and 13 and 14 are rejected under 35 USC 101 for the reasons already of record on pages 3-6 of the Office Action dated 9/10/03. That Office Action states:

A. Claims 1-3, 13 and 14 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility, or a well established utility. These claims are directed to an isolated nucleic acid comprising SEQ ID NO:1, nucleic acid molecules which encode the protein of SEQ ID NO:2, and which hybridize to SEQ ID NO:1, or to the complement thereof. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines (published 1/5/01, 66 FR 1092). The instant application has provided a nucleotide (SEQ ID NO:1) and protein (SEQ ID NO:2) sequence. However, the instant application does not disclose a specific and substantial biological role of the nucleic acid molecule of SEQ ID NO:1, the protein of SEQ ID NO:2, or their significance. Therefore, no specific and substantial utility of these nucleic acid molecules, or protein has be asserted.

It is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. Appellants disclose in the specification that the receptor encoded for by the claimed nucleic acid molecule is believed to encode a protein (termed "NHP" for "novel human protein") related to either eukaryotic phosphate or sugar transporters (page 15, lines 19-20). However, the basis that the receptor is disclosed in the specification to be homologous to these transporters is not predictive of use. There is little doubt that, after complete characterization, this protein will probably be found to have a

patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Appellants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate, obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotide of the invention (SEQ ID NO:1) encodes a protein which is "similar to eukaryotic phosphate or sugar transporters." However, this is not a specific and substantial asserted utility, or a well established utility of the protein of the instant specification. No comparisons between the sequence of the protein of the present invention and any eukaryotic phosphate or sugar transporters protein have been disclosed in the specification, nor does the specification disclose that the protein encoded for by the polynucleotide of the present invention has biological activities similar to either eukaryotic phosphate or sugar transporters. Sequence homology alone cannot be accepted in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (Trends in Biotech. 18:34-39, 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (Trends in Genetics 14:248-250, 1998) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a

new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (Nature Biotechnology 15:1222-1223, 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (Trends in Genetics 15:132-133, 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, most homologs must have different molecular and cellular functions. Finally, Bork et al. (Trends in Genetics 12:425-427, 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Therefore, based on the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:1, which is only known to encode a protein which "are similar to eukaryotic phosphate or sugar transporters."

Therefore, the instant claims are drawn to a nucleic acid molecule which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said nucleic acid molecule, or encoded protein, identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, or any significance of the nucleic acid molecule of the present invention, which has not been disclosed in the specification as having any specific or substantial utility, there is no immediately obvious patentable use for them. To employ the nucleic acid molecule of the instant invention to produce a receptor protein to identify substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for the nucleic acid molecule of the invention, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Therefore, since the nucleic acid molecule of the invention (SEQ ID NO:1), nor its encoded protein (SEQ ID NO:2), are supported by a specific and substantial asserted utility, or a well established utility, then polynucleotides encoding SEQ ID NO:2, as well as expression vectors and host cells comprising these nucleic acid molecule also do not possess a specific and substantial utility.

Appellants argue that the presently claimed protein is clearly referred to as a transporter protein and that these proteins transport material across the lipid bilayer. Appellants argue that this situation is not

analogous to Brenner v. Manson and that the function of transporters is well known. Appellants also argue that the references cited by the Examiner, on a whole, support the assertion that a protein's function can be (or is at least more likely than not) predicted based on homology and that, in the present situation, the function of transporter proteins are well-known.

These arguments have been considered, but are not deemed persuasive. Though Appellants have clearly stated that the protein of the present invention is a transporter protein and that homology, at times, may be used to predict the function of a protein, Appellants have still not provided any conclusive evidence that the protein of the present invention is a transport protein. Contrary to Appellicants' arguments, the Examiner is not implying that a real-world utility does not require further characterization, only that a patent is not a "hunting license." If Appellants were able to establish that the protein encoded for by the polynucleotide of the present invention was a specific type of transporter protein, then further characterization would be acceptable.

The use of the polynucleotide of the present invention in such applications as the Human Genome Project does not confer a specific use for the polynucleotide of the present invention, or its encoded protein. In other words, though the Human Genome Project itself may be substantial and credible, it does not provide a substantial or specific utility of the polynucleotide of the present invention. Similarly, the argument that the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins, or that uses such as "for DNA chips," "chromosomal mapping," or other "markers" is not persuasive since these uses, again, are neither specific or substantial since any nucleotide sequence can be used in such an assay. While it is clear that the nucleic acid molecule of the present invention would hybridize to a chromosome, without knowing the function of the protein encoded for by this nucleic acid molecule, then simply identifying that a nucleic acid molecule localizes to a particular region of a chromosome would not provide a substantial use for the nucleic acid molecule of the present invention. Finally, Appellants argue that the USPTO has issued numerous patents which appear to contain proteins with no identifiable functions. However, all issued patents are presumed to have a utility.

6. Claim Rejections - 35 USC § 112, first paragraph - enablement

Claims 1-3, 13 and 14 remain rejected for the reasons already of record on page 6 of the Office Action dated 9/10/02. That Action states:

A. Claims 1-3, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

In the Appeal Brief filed 10/23/03, Appellants argue that the protein of the present invention was clearly identified as a transporter protein which share structural similarity with mammalian sugar and sodium-dependent inorganic phosphate transporters. Appellants argue that this situation is not analogous to Brenner v. Manson and that the function of transporters is well known. Appellants also argue that the references cited by the Examiner, on a whole, support the assertion that a protein's function can be (or is at least more likely than not) predicted based on homology and that, in the present situation, the function of transporter proteins are well-known.

These arguments have been considered, but are not deemed persuasive. Though Appellants' have clearly stated that the protein of the present invention is a transporter protein and that homology, at times, may be used to predict the function of a protein, Appellants have still not provided any support other than homology that the protein of the present invention is a transport protein. The fact that the protein has no utility since it lacks 100% consensus on prediction is not the basis for the utility rejection. A protein can be less than 100% homologous to a known protein and have utility. Homology, alone, cannot be relied upon to predict protein function, as is the situation here. Therefore, regarding Brenner vs. Manson, even, *arguendo*, the situation was not analogous to the present situation, Appellants have still not demonstrated that the proteins of the present invention are, in fact, transporter proteins. Therefore, arguing that the present situation is not analogous to Brenner since transporters have a more specifically known function and mechanism than anticancer compounds is, respectfully, irrelevant. Regarding the references cited by the Examiner, the Examiner will state that the references as a whole demonstrate that it is difficult to make predictions about function with certainty. However, in the absence of any other support for the utility of the present invention as an inorganic phosphate transporter or sugar transporter, these references still support the Examiner's position. In fact, it is not clear which of the utilities the present invention is

claiming, since Appellants have argued that the protein of the present invention is homologus to both sugar transporters and sodium-dependent inorganic phosphate transporters. Therefore, in the absence of supporting evidence that the present invention is a transporter, in addition to the fact that Appellants are not certain which type of transporter is encoded by the present invention, the artisan would not find Applicants' claim believable. Though Appellants have shown that numerous databases, including InterPro, Pfam, ProtComp, SMART, TMHMM and ProDom support the finding that the protein of the present invention is a transporter, none of these results indicate to which family of transporters this protein belongs, nor, similarly, which types of molecules it transports, or in which direction, etc.

Appellants comparison of the present situation to that of Example 10 of the training guidelines is also not persuasive. The training example focuses on the fact that that protein of that invention is a DNA ligase. The difference between the training example and the present invention is that the function of DNA ligases are well known in the art and all DNA ligases have the same scope and function. In addition, the training example states that the protein in question is 95% homologous to known DNA ligases and only 50% identical to the next closest protein, alpha-actin. The present situation differs in that the function of one transporter cannot be extrapolated to the function of another. Again, different transporters would be expected to transport different substances. Therefore, the artisan would not be able to determine the specific utility of one transporter given another transporter, especially in light of the fact that the specification itself is not clear as to which family the alleged transporter belongs.

Appellants argue that the Examiner dismisses the assertion of 'gene chips' as a utility and argue that only a small number of nucleic acid molecules can be used to track gene expression since only a small number of nucleotide sequences are expressed. They further argue that expression profiling does not require a knowledge of the function of the particular nucleic acid on the gene chip and that the chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular types of tissues. First, what Appellants consider "a small number" includes thousands of nucleotide sequences and the fact that the artisan can determine the level of DNA expression among tissues is not a specific and substantial utility as a large number of DNA molecules can be used for this purpose. Appellants further argue that the Examiner has been confusing uniqueness and specificity. However, the Examiner is not arguing the specificity of the DNA itself, but rather its use. In other words, while the DNA itself *is* unique, the Examiner is not arguing that the DNA can have no utility since other DNA molecules are already known, but rather that the *use* of this DNA as a probe, or a marker is not a specific and substantial use and, therefore, itself is not sufficient to demonstrate utility unless the presence of an elevation or reduction of the DNA is correlated to a disease state. If this were the case, then anyone can obtain a patent

for an isolated strand of DNA by simply asserting that the DNA can be used as a probe, or marker. This, respectfully, is analogous to saying transgenic mice have utility since they can be used as snake food. This would not be a specific utility since nearly every transgenic mouse could be used as snake food.

Additionally, Appellants' argument that SEQ ID NO:1, the sequence of the present invention, can be used to map the 13 coding exons of chromosome 20q is also not a specific or substantial utility. Though only a small percentage of nucleotide sequences are located in this region of chromosome 20q, virtually any DNA can be used to map coding exons on chromosomes in general and this information, respectfully, does not provide any specific and substantial utility to the protein itself, nor have Appellants disclosed any disease states which map to this locus. Furthermore, this mapping was not disclosed in the specification as originally filed. Therefore, Appellants are able to conclude that the DNA encoding the protein of the present invention maps to chromosome 20q, but no pertinent information can be obtained from this knowledge, especially in view of its submission subsequent to filing.

Appellants further cite *In re Brana*, their major argument being that "further research does not preclude a finding that the invention has utility" and that "further research and development" is (may be) necessary. However, Appellants' reliance on *In re Brana* is misplaced. That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well-established specific and substantial utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive in vitro data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. The protein of the instant invention has not been shown in the specification as originally filed to belong to a family of compounds with a common well-established specific and substantial utility. Appellants state that protein of the invention is a transporter, but it is not clear if it is a sugar transporter, a sodium-dependent inorganic phosphate transporter, or another type of transporter. Unlike Brana, Appellants do not provide any in vitro data, or any data correlating to the use of these compounds in vivo. Since the instant specification does not disclose the protein of the present invention as being a specific transporter, the disclosure that it is only believed to be a member of this family, which comprises a large number of subfamilies is not particularly useful.

Furthermore, In re Brana, as stated by Appellants, is concerned mainly with the utility of *pharmaceutical compositions* whereas the present invention is concerned with the utility of receptor *proteins*. Appellants make no mention in their arguments of Brana that the compounds, themselves, to be used in the pharmaceutical compositions do not have utility. Appellants only state that Brana is concerned with the *pharmaceutical compositions* comprising these compounds. Appellants discuss the significance

of the FDA and Phase II testing regarding Brana. However, these issues are not relevant in this situation. If Appellants were claiming that the protein of the present invention, or nucleic acids encoding these proteins, could be used in pharmaceutical compositions, that may be considered analogous. However, the proteins themselves would first need to possess utility in order for the pharmaceutical composition to possess utility. Since the proteins of the present invention do not possess utility, any comparison to Brana is, respectfully, irrelevant. As stated on page 5 of the Office Action dated 9/10/02, a patent is not a hunting license. This same statement can be made with regard to Appellants' argument using *In re Angstadt and Griffin*. Appellants state that "the need for some experimentation does not render the claimed invention unpatentable." However, experimentation only refers to enablement, not utility. No further experimentation should be required. The invention is based on only what is disclosed in the specification. The instant specification is that the protein is believed to be a transporter, with no further support of utility. Finally, Appellants argue that numerous patents have been issued over the years which do not comply with the new Utility Guidelines. The Examiner states that issued US Patents are presumed to meet all of the requirements for patentability.

Finally, though not argued by Appellants in the body of the Brief, the summary of their invention in the Brief states that the use of the present invention to diagnose obesity, high blood pressure, connective tissue disorders and infertility. The Examiner wants to make of record the fact that Appellants have not demonstrated the use of the present invention in this manner.

Claim Rejections - 35 USC § 112, first paragraph – enablement

Claims 1-3, 13 and 14 are rejected under 35 USC 112, first paragraph, for the reasons already of record on page 6 of the Office Action dated 9/10/02 as well as for the reasons given in the above rejection under 35 USC 101. Appellants argue that the claimed invention is enabled because it has utility as argued previously. Appellants' arguments have been fully considered, but are not found to be persuasive for the reasons discussed above.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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December 01, 2003

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